



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 880

[Docket No. FDA-2013-M-0042]

Medical Devices; General Hospital and Personal Use Monitoring Devices; Classification of the Ingestible Event Marker

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA) is classifying the ingestible event marker into class II (special controls). The Agency is classifying the device into class II (special controls) in order to provide a reasonable assurance of safety and effectiveness of the device.

DATES: This order is effective [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. The classification was applicable beginning July 10, 2012.

FOR FURTHER INFORMATION CONTACT: James Cheng, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm 1326, Silver Spring, MD 20993-0002, 301-796-6306.

SUPPLEMENTARY INFORMATION:

I. Background

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360c(f)(1)), devices that were not in commercial distribution before May 28, 1976 (the date of enactment of the Medical Device Amendments of 1976), generally referred to as postamendments devices, are classified automatically by statute into class III without any

FDA rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II, or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807) of the regulations.

Section 513(f)(2) of the FD&C Act, as amended by section 607 of the Food and Drug Administration Safety and Innovation Act (Public Law 112-144, July 9, 2012, 126 Statute 1054), provides two procedures by which a person may request FDA to classify a device under the criteria set forth in section 513(a)(1). Under the first procedure, the person submits a premarket notification under section 510(k) of the FD&C Act for a device that has not previously been classified and, within 30 days of receiving an order classifying the device into class III under section 513(f)(1) of the FD&C Act, the person requests a classification under section 513(f)(2). Under the second procedure, rather than first submitting a premarket notification under section 510(k) and then a request for classification under the first procedure, the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence and requests a classification under section 513(f)(2) of the FD&C Act. If the person submits a request to classify the device under this second procedure, FDA may decline to undertake the classification request if FDA identifies a legally marketed device that could provide a reasonable basis for review of substantial equivalence with the device or if FDA determines that the device submitted is not of “low-moderate risk” or that general controls would be inadequate to control the risks and special controls to mitigate the risks cannot be developed.

In response to a request to classify a device under either procedure provided by section 513(f)(2) of the FD&C Act, FDA will classify the device by written order within 120 days. This classification will be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing this classification.

In accordance with section 513(f)(1) of the FD&C Act, FDA issued an order on May 7, 2012, classifying the Proteus Personal Monitor including ingestible event marker into class III, because it was not substantially equivalent to a device that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or a device which was subsequently reclassified into class I or class II. On May 14, 2012, Proteus Biomedical, Inc., submitted a petition requesting classification of the Proteus Personal Monitor including ingestible event marker under section 513(f)(2) of the FD&C Act. The manufacturer recommended that the device be classified into class II (Ref. 1).

In accordance with section 513(f)(2) of the FD&C Act, FDA reviewed the petition in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the FD&C Act. FDA classifies devices into class II if general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the petition and the medical literature, FDA determined that the device can be classified into class II with the establishment of special controls. FDA believes these special controls will provide reasonable assurance of the safety and effectiveness of the device.

The device is assigned the generic name ingestible event marker, and it is identified as a prescription device used to record time-stamped, patient-logged events. The ingestible component links wirelessly through intrabody communication to an external recorder which records the date and time of ingestion as well as the unique serial number of the ingestible device.

FDA has identified the following risks to health associated with this type of device and the measures required to mitigate these risks:

Table 1.--Ingestible Event Marker Risks and Mitigation Measures

Identified Risks	Mitigation Measures
Adverse tissue reaction	Biocompatibility Testing Labeling (dose limits)
Systemic toxicity	Toxicology Testing Labeling (dose limits)
Electromagnetic incompatibility	Electromagnetic Compatibility Testing Wireless Testing Labeling
Electrical safety issues	Electrical Safety Testing Labeling
Electrical/Mechanical failure	Nonclinical Performance Testing
Failure to mark event	Nonclinical Performance Testing Clinical Evaluation
Failure to excrete	Animal Testing
Usability	Human Factors Testing

	Labeling
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FDA believes that the following special controls, in addition to the general controls, address these risks to health and provide reasonable assurance of safety and effectiveness:

1. The device must be demonstrated to be biocompatible and non-toxic;
2. Nonclinical, animal, and clinical testing must provide a reasonable assurance of safety and effectiveness, including device performance, durability, compatibility, usability (human factors testing), event recording, and proper excretion of the device;
3. Appropriate analysis and nonclinical testing must validate electromagnetic compatibility performance, wireless performance, and electrical safety; and
4. Labeling must include a detailed summary of the nonclinical and clinical testing pertinent to use of the device and the maximum number of daily device ingestions.

Ingestible event markers are prescription devices restricted to patient use only upon the authorization of a practitioner licensed by law to administer or use the device. (Proposed § 880.6305(a) (21 CFR 880.6305(a)); see section 520(e) of the FD&C Act (21 U.S.C. 360j(e)) and § 801.109 (21 CFR 801.109) (Prescription devices).) Prescription-use restrictions are a type of general controls authorized under section 520(e) and defined as a general control in section 513(a)(1)(A)(i) of the FD&C Act.

Therefore, on July 10, 2012, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying the classification of the device by adding § 880.6305.

Following the effective date of this final classification administrative order, any firm submitting a 510(k) premarket notification for an ingestible event marker will need to comply with the special controls named in the final administrative order.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For this type of device, FDA has determined that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device. Therefore, this device type is not exempt from premarket notification requirements. Persons who intend to market this type of device must submit to FDA a premarket notification prior to marketing the device, which contains information about the ingestible event marker they intend to market.

II. Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

III. Paperwork Reduction Act of 1995

This final administrative order establishes special controls that refer to previously approved collections of information found in other FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in part 807, subpart E, regarding premarket notification submissions have been approved under OMB control number 0910-0120, and the collections of information in 21 CFR part 801, regarding labeling, have been approved under OMB control number 0910-0485.

IV. Reference

The following reference has been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and is available electronically at <http://www.regulations.gov>.

1. Petition: Request for Evaluation of Automatic Class III Designation Under Section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act From Proteus Biomedical, Inc., dated May 9, 2012.

List of Subjects in 21 CFR Part 880

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 880 is amended as follows:

PART 880--GENERAL HOSPITAL AND PERSONAL USE DEVICES

1. The authority citation for 21 CFR part 880 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Add § 880.6305 to subpart G to read as follows:

§ 880.6305 Ingestible event marker.

(a) Identification. An ingestible event marker is a prescription device used to record time-stamped, patient-logged events. The ingestible component links wirelessly through intrabody communication to an external recorder which records the date and time of ingestion as well as the unique serial number of the ingestible device.

(b) Classification. Class II (special controls). The special controls for this device are:

(1) The device must be demonstrated to be biocompatible and non-toxic;

(2) Nonclinical, animal, and clinical testing must provide a reasonable assurance of safety and effectiveness, including device performance, durability, compatibility, usability (human factors testing), event recording, and proper excretion of the device;

(3) Appropriate analysis and nonclinical testing must validate electromagnetic compatibility performance, wireless performance, and electrical safety; and

(4) Labeling must include a detailed summary of the nonclinical and clinical testing pertinent to use of the device and the maximum number of daily device ingestions.

Dated: May 10, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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